57. REMARKS/ARGUMENTS

Claims 47-56 are currently pending in this application. Applicants have amended claim 47, 53-54, and 56 to more distinctly claim that which Applicants regard as their invention. No new matter has been introduced by this amendment.

Applicants offer the following remarks in order to expedite prosecution.

I. Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 53-56 have been rejected as lacking enablement because BCR and TCR are not found on mast cells or basophils. The Office further states that the "skilled artisan would not be able to find a nexus between the applicant's working examples concerning the cross-linking of FcεRI and FcγRIIB or FcεRII on mast cells and the cross linking of BCR or TCR with either FcγRIIB or FcεRII." (Office Action at page 4).

In order to expedite prosecution and clarify the invention Applicants have amended claims 53 and 54 to remove BCR and TCR. However, Applicants have not amended claim 56 and respectfully traverse the Office's statement regarding nexus. Applicants have disclosed a correlation between various ITAMs and ITIMs. These motifs have been shown to be conserved and it has been shown that an ITAM motif is activating and ITIMs are inhibitory. Applicants have also demonstrated that the bispecific antibodies of the Examples are able to inhibit the function of the ITAM by cross-linking it to the ITIM. It is well known that TCR and BCR are involved in cytokine release upon activation, and that there is a correlation between cytokine release and allergic disease. Therefore, there is a nexus between demonstrating that cross-linking of an ITAM with an ITIM on the surface of a mast cell and the cross-linking of an ITAM and an ITIM of the surface of a B-cell or a T-cell. Applicants have demonstrated the construction of such bispecific molecules and a method of testing for the inhibition of the ITAM by cross-linking. It would not require undue experimentation to construct a bispecific molecule capable of cross-linking a BCR or TCR with either FcγRIIB or FcεRII given the guidance provided by Applicants' specification. Applicants have demonstrated that the antibody is capable of cross-linking, no further guidance is needed to practice the full scope of the claims.

Therefore, Applicants submit that the rejection should be withdrawn.

II. Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 47 has been rejected as being indefinite due to the recitation of FcγRIII. Applicants have amended Claim 47 to more particularly and distinctly claim the specific ITIMs and ITAMs. Therefore, this rejection is now moot and should be withdrawn.

Claim 50 has been rejected as lacking antecedent basis for the phrase "the ITIM is FcγRII." Applicants have amended claim 50 to recite FcγRIIB and request that the rejection be withdrawn.

Claim 55 has been rejected as lacking antecedent basis for the phrase 'bispecific antibody concentration". Applicants have amended the claim as the Office suggests and request that th rejection be withdrawn.

III. Rejections Under 35 U.S.C. § 102(b)

Claims 47-48 and 51 have been rejected as anticipated by Vossebeld et al. The Office alleges that Vossebeld teach a bispecific antibody comprising an ITAM and ITIM.

Applicants disagree with the interpretation of the reference. In actuality, the reference shows the colligation of two ITAM receptors and their subsequent activation as demonstrated by calcium influx. However, this rejection has been rendered moot by the amendment of claim 47 and should be withdrawn.

IV. Rejections Under 35 U.S.C. § 103(a)

Claims 47-48 and 50-56 have been rejected as unpatentable over Katz et al. In view of Daeron et al. (EP 0 861 891). The Office alleges that Katz teach that mast cells contain ITIMs inhibit mast cell activation following co-ligation with the ITAM FcεRI. The Office admits that Katz do not teach inhibition using a bispecific antibody. The Office alleges that Daeron teaches co-aggregation of the ITAM FcεRI and the ITIM FcγRIIB. Applicants respectfully traverse this rejection.

Katz et al. merely recognize that there is a mast cell homeostasis resulting from inhibition of activation by receptors on the surface. There is no suggestion that these receptors can be artificially cross-linked by adding a bispecific antibody. To establish a *prima facie* case of obviousness, the Office must show a suggestion or motivation in the reference to combine the teachings to arrive at the claimed invention. Katz does not provide this motivation. Moreover, Daeron et al. teaches away from the current invention

by stating that other ITIMs do not function in the same manner as KIR, and he specifically highlights the differences between KIR and other ITIMs, such as FcγRIIB (See, e.g., example II).

Therefore, the Office has failed to establish a suggestion or motivation to combine the references and thus has failed to establish a *prima facie* case of obviousness. In view of these remarks, Applicants submit that this rejection should be withdrawn.

Conclusion

In view of the foregoing remarks, Applicants assert that the application is in condition for allowance and request a notice of same.

Respectfully Submitted,

Dated: August 19, 2005.

BY: Cheryl A. Liljestrand
Cheryl A. Liljestrand
Reg. No. 45,275